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ABSTRACTS IN CARDIOLOGY

Variable response to vasodilators in primary pulmonary hypertension

Rich and colleagues have previously reported the use of high dose calcium-channel blocking therapy for primary pulmonary hypertension and provided evidence for a long-term reduction in pulmonary arterial pressure (*Circulation* 1987;**76**:135–41). They now write about the effect of these high doses on survival after five years. It is no surprise that their treated patients did better. They were less ill. Such patients presumably have pulmonary arteries that are more muscular and capable of dilating so that cardiac output can increase and systemic blood pressure is maintained. Rich *et al* compare their less severely affected patients with the commoner, more severely affected patients who were likely to do badly. The much smaller doses of calcium channel blockers that can be taken by "non-responders" may still be beneficial; but this is harder to prove. Unless they feel considerable benefit patients will not tolerate the painful puffy legs that are an unsightly consequence of high dose treatment with these agents.

Rich *et al* only gave warfarin to patients with non-uniform perfusion lung scans and they claim that this particularly helped "non-responders". Most patients with primary pulmonary hypertension have uniform lung scans, but soft patchy defects are sometimes seen—though they look quite different from the stark segmental defects seen in patients with major vessel occlusions. I have long believed and advocated the use of long-term warfarin. This may prevent secondary thrombosis in a pulmonary vascular bed with endothelial damage but also has a major role in patients whose very low flows make them vulnerable to venous thromboembolism.

Primary pulmonary hypertension is not uniformly progressive. All patients should have their response to vasodilator drugs evaluated. I believe that calcium-channel blocking agents should be given in the maximum tolerated doses to all patients who will take them, the response to acute administration being a guide both to prognosis and to dose. I also believe that all patients with this diagnosis should be given long-term anticoagulants.

CELIA M OAKLEY

The effect of high doses of calcium-channel blockers on survival in primary pulmonary hypertension

Stuart Rich, Elizabeth Kaufmann, Paul S Levy

Abstract

Background.—Primary pulmonary hypertension is a progressive, fatal disease of unknown cause. Vasodilator drugs have been used as a treatment, but their efficacy is uncertain.

Methods.—We treated 64 patients with primary pulmonary hypertension with high doses of calcium-channel blockers. Patients who responded to treatment (defined as those whose pulmonary-artery pressure and pulmonary vascular resistance immediately fell by more than 20 per cent after challenge) were treated for up to five years. Their survival was compared with that of the patients who did not respond and with patients enrolled in the National Institutes of Health (NIH) Registry on Primary Pulmonary Hypertension. Warfarin was given to 55 per cent of the patients as concurrent therapy, on the basis of a lung scan showing nonuniformity of pulmonary blood flow (47 per cent of patients who responded and 57 per cent of those who did not respond).

Results.—Seventeen patients (26 per cent) responded to treatment, as indicated by a 39 per cent fall in pulmonary-artery pressure and a 53 per cent fall in the pulmonary-vascular-resistance index ($P < 0.001$). Nifedipine (mean [$\pm$SD] daily dose, 172 $\pm$ 41 mg) was given to 13 patients, and diltiazem (mean daily dose, 720 $\pm$ 208 mg) was given to 4 patients. After five years, 94 per cent of the patients who responded (16 and 17) were alive, as compared with 55 per cent of the patients who did not respond (26 of 47, $P = 0.003$). The survival of the patients who responded was also significantly better than that of the NIH registry cohort ($P = 0.002$) and patients from the NIH registry who were treated at the University of Illinois ($P = 0.001$). The use of warfarin was associated with improved survival ($P = 0.025$), particularly in the patients who did not respond.

Conclusions.—This study suggests that high doses of calcium-channel blockers in patients with primary pulmonary hypertension who respond with reductions in pulmonary-artery pressure and pulmonary vascular resistance may improve survival over a five-year period. (*N Engl J Med* 1992;**327**: 76–81.)